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Laparoendoscopic single-site donor nephrectomy (LESS-N) versus standard laparoscopic donor nephrectomy (Protocol)

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[Intervention Protocol]

Laparoendoscopic single-site donor nephrectomy (LESS-N) versus standard laparoscopic donor nephrectomy

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

This review aims to look at the benefits and harms of LESS-N compared with the current standard of laparoscopic nephrectomy for patients undergoing organ donation.

BACKGROUND

Laparoscopic nephrectomy for benign kidney conditions was first performed in 1991 (Clayman 1991) and laparoscopic donor nephrectomy was successfully initiated in 1995 (Ratner 1995). In the years since, laparoscopic nephrectomy for both benign disease and organ donation has become the technique of choice in most major academic centres worldwide (Canes 2010; Kaouk 2011; Kurien 2011; Ramasamy 2011). Laparoscopic nephrectomy has gained popularity due to decreased morbidity, better quality of life, shorter hospital stay, rapid recovery period and return to normal daily activities, better cosmetic results, and reduced postoperative pain when compared with open nephrectomy (Kok 2006; Kurien 2011; Tugcu 2010).

Description of the condition

Simple nephrectomy procedures are being conducted for benign conditions such as renovascular hypertension, chronic pain syndromes (symptomatic acquired renal cystic disease, loin pain/haematuria syndrome), chronic infection processes (chronic pyelonephritis, xanthogranulomatous pyelonephritis, renal tuberculosis), in addition to live donor nephrectomy for kidney transplantation (Walsh 2012). Because nephrectomy for transplantation involves live donors, reducing postoperative morbidity is paramount; hence, laparoscopic donor nephrectomy has become the preferred technique in many transplant units (Walsh 2012).

Description of the intervention

Laparoendoscopic surgery is the natural evolution of laparoscopic surgery and has been made possible by the development of laparoscopic technology and instruments, in addition to increasing surgical skills (Granberg 2010). This was made possible by the development of multichannel single ports and curved articulating instruments (Canes 2010; Granberg 2010). Though various terms have been used to describe this method, the LaparoEndoscopic Single Site Surgery Consortium for Assessment and Research has agreed on 'laparoendoscopic single-site surgery' (LESS) (Tugcu 2010). Several centres have published their results of LESS nephrectomy (LESS-N), partial nephrectomy, pyeloplasty, and many other urological procedures (Canes 2010; Kaouk 2011; Kurien 2011; Park 2011; Tugcu 2010; Walsh 2012). Rane 2007 first described a single port nephrectomy in 2007 which could potentially replace standard laparoscopy.

How the intervention might work

LESS-N has been reported to be a safe and effective alternative to laparoscopic nephrectomy with better cosmetic results and less postoperative pain (Canes 2010; Kurien 2011; Ramasamy 2011; Tugcu 2010). However, these advantages have only been reported from small cohort studies. While its benefit might be greater for cosmetic results, as shown in a survey conducted by Park 2011, other studies of patients who underwent LESS-N compared to laparoscopic and open kidney surgery found that there was a significant overall benefit of LESS-N over these two modalities (Desai 2011; Kaouk 2011). However, a comparison of complications of LESS-N versus laparoscopic nephrectomy using the modified Clavien grading system found that LESS-N was as safe as laparoscopic nephrectomy with similar postoperative outcomes and low morbidity (Ramasamy 2011).

The reduced morbidity of laparoscopic donor nephrectomy has encouraged more potential donors to be evaluated for surgery and, if LESS-N can be shown to safely offer significant benefits, then more patients might benefit from the further expansion of the live donor pool (Canes 2010). Furthermore, LESS-N can provide a safe and effective alternative to laparoscopic nephrectomy for patients suffering from benign kidney disease such as xanthogranulomatous pyelonephritis, symptomatic renal cysts, and ureteropelvic junction obstruction, as the resection specimen can be easily removed through a single port (Permpongkosol 2011).

Why it is important to do this review

Though dialysis is an alternative in patients with end-stage kidney disease, the accompanying increase in morbidity and mortality greatly reduces the long term survival of these patients (Gajdos 2013; Suzuki 2012; Unsal 2012). Therefore, kidney transplantation is vital for these patients to allow for a potentially longer survival. To ensure live donor organs are available, methods for reducing convalescence, postoperative complications, and improving cosmetic results are essential. This might lead to more willing donors (Canes 2010; Soliman 2011). These methods include laparoscopic surgery and potentially more so single-site laparoscopic surgery. The quicker recovery period and reduced pain attributed to these surgical techniques (LESS-N and laparoscopic nephrectomy) can improve the immediate postoperative quality of life for both donor patients and those who undergo the procedure for benign disease. Evaluating the difference between LESS-N and laparoscopic nephrectomy in patients undergoing the procedures for both benign disease as well as live kidney donation will indicate which procedure is optimal in improving these factors.

OBJECTIVES

This review aims to look at the benefits and harms of LESS-N compared with the current standard of laparoscopic nephrectomy for patients undergoing organ donation.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) and quasi-RCTs (RCTs in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) looking at comparisons of LESS-N and laparoscopic nephrectomy.

Types of participants

Inclusion criteria

All adult patients undergoing nephrectomy for live organ donation.

Exclusion criteria

Studies on children, patients undergoing a nephrectomy for cancer, or a comparison of LESS-N to any other procedure other than laparoscopic nephrectomy will be excluded. In addition to abstract publication and reports from meetings will also be excluded.

Types of interventions

The intervention is LESS-N compared to laparoscopic donor nephrectomy, conducted by the same surgical team with an experience laparoscopist (who has surpassed their learning curve for the procedure) leading the procedure.

Types of outcome measures

1. Patient demographics (age, sex, body mass index, ASA score)
2. Operative information (operative time, blood loss, conversion rates, hospital stay, approach (transperitoneal or retroperitoneal))
3. Kidney function measures (pre- and postoperative creatinine course and glomerular filtration rate (GFR))
4. Quality of life issues (pain scores, time taken to return to normal activity, body image satisfaction)
5. Adverse events and complications either intra- or postoperative
6. Mortality
7. For donor nephrectomy: survival of the graft.

Primary outcomes

The primary outcomes will be the operative and postoperative parameters compared between the two groups.

1. Operative times
2. Estimated intraoperative blood loss
3. Postoperative pain scores
4. Complications.

Secondary outcomes

Secondary outcomes will focus on the quality of life issues, kidney function deterioration post nephrectomy, and cost analysis comparing between the two groups.

1. Length of hospitalisation
2. Length of time to return to normal activities
3. Blood transfusion rates
4. Conversion rates
5. Analgesic requirement postoperatively
6. Warm ischaemia time
7. Length of surgical wound, trocar size used
8. Graft survival
9. Cost analysis.

Search methods for identification of studies

Electronic searches

We will search the Cochrane Renal Group's Specialised Register through contact with the Trials' Search Co-ordinator using search terms relevant to this review. The Cochrane Renal Group's Specialised Register contains studies identified from the following sources.

1. Monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL)
2. Weekly searches of MEDLINE OVID SP
3. Handsearching of renal-related journals and the proceedings of major renal conferences
4. Searching of the current year of EMBASE OVID SP
5. Weekly current awareness alerts for selected renal journals
6. Searches of the International Clinical Trials Register (ICTRP) Search Portal and ClinicalTrials.gov.

Studies contained in the Specialised Register are identified through search strategies for CENTRAL, MEDLINE, and EMBASE based on the scope of the Cochrane Renal Group. Details of these strategies, as well as a list of handsearched journals, conference proceedings and current awareness alerts, are available in the Specialised Register section of information about the Cochrane Renal Group. See Appendix 1 for search terms used in strategies for this review.

Searching other resources

1. Reference lists of clinical practice guidelines, review articles and relevant studies.
2. Letters seeking information about unpublished or incomplete studies to investigators known to be involved in previous studies.

Data collection and analysis

Selection of studies

The search strategy described will be used to obtain titles and abstracts of studies that may be relevant to the review. The titles and abstracts will be screened independently by three authors who will discard studies that are not applicable; however, studies and reviews that might include relevant data or information on studies will be retained initially. Three authors will independently assess retrieved abstracts and, if necessary the full text, of these studies to determine which studies satisfy the inclusion criteria.

Data extraction and management

Data extraction will be carried out independently by three authors using standard data extraction forms. Studies reported in non-English language journals will be included if translation is possible (e.g. via web-based translation tools) and the data can be extracted. Where more than one publication of one study exists, reports will

be grouped together and only the publication with the most complete data will be used in the analyses. Where relevant outcomes are only published in earlier versions these data will be used. Any discrepancy between published versions will be highlighted. Any disagreement will be resolved by consensus or arbitration by two authors.

Assessment of risk of bias in included studies

The following items will be independently assessed by three authors using the risk of bias assessment tool (Higgins 2011) (see Appendix 2).

- Was there adequate sequence generation (selection bias)?
- Was allocation adequately concealed (selection bias)?
- Was knowledge of the allocated interventions adequately prevented during the study (detection bias)?
    - Participants and personnel
    - Outcome assessors
- Were incomplete outcome data adequately addressed (attrition bias)?
- Are reports of the study free of suggestion of selective outcome reporting (reporting bias)?
- Was the study apparently free of other problems that could put it at a risk of bias?

Measures of treatment effect

Dichotomous outcomes, such as patient demographics, complications, blood transfusion rates, conversion rates, and graft survival, will be expressed as risk ratios (RR) with 95% confidence intervals (CI). Continuous outcomes, such as operative times, blood loss, postoperative pain scores, length of hospital stay, length of time to return to normal activities, and cost analysis will be expressed as mean difference (MD) or SMD if different scales (e.g. pain scores) have been used.

Unit of analysis issues

Only simple parallel group designs are available for this surgical technique comparison.

Dealing with missing data

Any further information required from the original author will be requested by written correspondence (e.g. emailing the corresponding author) and any relevant information obtained in this manner will be included in the review. Evaluation of important numerical data such as screened, randomised patients as well as intention-to-treat, as-treated and per-protocol population will be carefully performed. Attrition rates, for example drop-outs, losses to follow-up and withdrawals will be investigated. Issues of missing data and imputation methods (e.g. last-observation-carried-forward) will be critically appraised (Higgins 2011).

Assessment of heterogeneity

Heterogeneity will be analysed using a Chi² test on N-1 degrees of freedom, with an alpha of 0.05 used for statistical significance and with the I² test (Higgins 2003). I² values of 25%, 50% and 75% correspond to low, medium and high levels of heterogeneity.

Assessment of reporting biases

If possible, funnel plots will be used to assess for the potential existence of small study bias (study effects versus study size) (Higgins 2011).

Data synthesis

Data will be pooled using the random-effects model but the fixed-effect model will also be used to ensure robustness of the model chosen and susceptibility to outliers.

Subgroup analysis and investigation of heterogeneity

A subgroup analysis will be used to explore possible sources of heterogeneity (e.g. participants, analyses of the impact of studies with poor methodology on the final result). Heterogeneity among participants could be related to demographics such as age and weight. Heterogeneity in treatments could be related to experience of the operating surgeon or assisting staff. Where possible, the risk difference with 95% CI will be calculated for each outcome.

Sensitivity analysis

We will perform sensitivity analyses to explore the influence of the following factors on effect size:

- repeating the analysis taking account of risk of bias
- repeating the analysis excluding any very long or large studies to establish how much they dominate the results
- repeating the analysis excluding studies using the following filters:
    - diagnostic criteria
    - language of publication
    - source of funding (industry versus other)
    - country
    - conversion rate
    - donation versus kidney disease nephrectomy
    - extraction site

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Desai 2011

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Suzuki 2012

Suzuki H, Hoshi H, Inoue T, Kikuta T, Tsuda M, Takenaka T. Early start of combination therapy with hemodialysis and peritoneal dialysis prolongs survival and reduces cardiovascular events in male patients. *Advances in Peritoneal Dialysis* 2012;**28**:68–73. [MEDLINE: 23311217]

Tugcu 2010

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Unsal 2012

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Walsh 2012

Wein A, Kavoussi L, Novick A, Partin A, Peters C (editors). *Campbell-Walsh Urology*. 10th Edition. Vol. **2**, Philadelphia: Elsevier Saunders, 2012.

* *Indicates the major publication for the study*

APPENDICES

Appendix 1. Electronic search strategies

Database	Search terms
CENTRAL	1. MeSH descriptor Nephrectomy, this term only 2. (laparoscopic NEAR/5 nephrectom*):ti,ab,kw in Trials 3. (laparoendoscopic single site surgery):ti,ab,kw in Trials 4. (LESS-N):ti,ab,kw in Trials 5. (LESS NEXT nephrectom*):ti,ab,kw in Trials 6. (#1 OR #2 OR #3 OR #4 OR #5)
MEDLINE	1. Nephrectomy/ 2. (laparoscopic adj5 nephrectom$).tw. 3. "laparoendoscopic single site surgery".tw. 4. "LESS-N".tw. 5. (LESS adj nephrectom$).tw. 6. or/1-5
EMBASE	1. exp nephrectomy/ 2. (laparoscopic adj5 nephrectom$).tw. 3. "laparoendoscopic single site surgery".tw. 4. "LESS-N".tw. 5. (LESS adj nephrectom$).tw. 6. or/1-5

Appendix 2. Risk of bias assessment tool

Potential source of bias	Assessment criteria
Random sequence generation Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence	*Low risk of bias:* Random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random)
	High risk of bias: Sequence generated by odd or even date of birth; date (or day) of admission; sequence generated by hospital or clinic record number; allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory test or a series of tests; by availability of the intervention
	Unclear: Insufficient information about the sequence generation process to permit judgement
Allocation concealment Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment	*Low risk of bias:* Randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study (e.g. central allocation, including telephone, web-based, and pharmacy-controlled, randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes)
	High risk of bias: Using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure
	Unclear: Randomisation stated but no information on method used is available
Blinding of participants and personnel Performance bias due to knowledge of the allocated interventions by participants and personnel during the study	*Low risk of bias*: No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken
	High risk of bias: No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding
	Unclear: Insufficient information to permit judgement

(*Continued*)

Blinding of outcome assessment Detection bias due to knowledge of the allocated interventions by outcome assessors	*Low risk of bias:* No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken
	High risk of bias: No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding
	Unclear: Insufficient information to permit judgement
Incomplete outcome data Attrition bias due to amount, nature or handling of incomplete outcome data	*Low risk of bias:* No missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods
	High risk of bias: Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation
	Unclear: Insufficient information to permit judgement
Selective reporting Reporting bias due to selective outcome reporting	*Low risk of bias:* The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon)

(*Continued*)

	High risk of bias: Not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study
	Unclear: Insufficient information to permit judgement
Other bias Bias due to problems not covered elsewhere in the table	*Low risk of bias:* The study appears to be free of other sources of bias.
	High risk of bias: Had a potential source of bias related to the specific study design used; stopped early due to some data-dependent process (including a formal-stopping rule); had extreme baseline imbalance; has been claimed to have been fraudulent; had some other problem
	Unclear: Insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias

CONTRIBUTIONS OF AUTHORS

1. Draft the protocol: OMA
2. Study selection: OMA, KA,
3. Extract data from studies: OMA, KA,
4. Enter data into RevMan: OMA
5. Carry out the analysis: OMA,
6. Interpret the analysis: OMA, HK
7. Draft the final review: OMA, PC, HK
8. Disagreement resolution: PD, HK
9. Update the review: OMA

DECLARATIONS OF INTEREST

None known.

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